REMARKS

Applicants would like to thank Examiner Cook for the courtesy of the Telephone Interview on February 6, 2007.

Claims 1-7, 16-18, 20-28, 31, 34, 35 and 37-41 are pending in the instant application. Claims 1-7, 16-18, 20-28, 31, 34, 35 and 37-41 have been rejected. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims under 35 U.S.C. 103(a)

Claims 1, 16-18, 20-27, 31 and 34 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Solaro et al. (Journal of Molecular Cell Cardiology, Vol. 28, pages 217-230, 1996) in view of Lin et al. (The Journal of Biological Chemistry, Vol. 271, No. 1, 1/5/1996, pages 244-249) and further in view of Han et al. (International Journal of Biochemistry, Vol. 24, No. 1, 1992, pages 19-28).

Claims 2-7, 28, 34-35, 38 and 40-41 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Solaro et al. in view of Lin et al. and further in view of Han et al. as applied to claims 1, 16-18, 20-27 and 34 above, and further in view of Wicks et al. (U.S. Patent 5,834,220).

Claims 37 and 39 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Solaro et al. in view of Lin et al. and further in view of Han et al. as applied to

claims 1, 16-18, 20-27 and 34 and Wicks et al. (U.S. Patent 5,834,220) as applied to claims 2-7, 28, 34-35, 38 and 40-41 above, and further in view of Jideama et al. (The Journal of Biological Chemistry, Vo. 271, No. 38, 9/20/96, pages 23277-23283).

Applicants respectfully traverse these rejections.

With respect to the combination of Solaro et al. in view of Lin et al. and further in view of Han et al., the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to measure myofilament chemical adducts as taught by Lin et al. in the detection method of Solaro et al. because Lin et al. taught that chemical adduct modifications exhibited inhibition of myofibril activity. The Examiner has acknowledged that both Solaro et al. and Lin et al. are silent with respect to the myofilament protein modification product being a post-translational modification. However, the Examiner suggests that Han et al. teach that post-translational modifications involve the making or breaking of covalent bonds, that post-translational modifications are varied and include phosphorylation, that numerous post-translational modifications are recognized in a wide variety of cell types, and that each modification serves a useful role. Thus, the Examiner suggests that it would have been

obvious to one having ordinary skill in the art at the time of the invention to detect post-translational modifications, in order to evaluate protein-ligand interaction, subcellular organization, assembly of bimolecular complexes, regulation of catalytic activity and/or protein turnover.

It is respectfully pointed out, however, that the claims are not drawn to detecting post-translational modification, in order to evaluate protein-ligand interaction, subcellular organization, assembly of bimolecular complexes, regulation of catalytic activity and/or protein turnover.

Rather, the claims are drawn to a method for **assessing cardiac or skeletal muscle damage in a subject** by evaluating for the presence of a post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins selected from the group consisting of troponin I, troponin T, troponin C, α-actinin and myosin light chain 1, wherein the presence of at least one of these myofilament protein modification products in the biological sample **is indicative of cardiac or skeletal muscle damage in said subject.** No where do any of

the cited references of Solaro et al., Lin et al. or Han et al. teach or suggest assessing cardiac or skeletal damage via detection of the presence of a myofilament protein modification product as claimed. Thus, the cited references of Solaro et al., Lin et al. and Han et al., none of which are related to assessing cardiac or skeletal muscle damage, clearly provide no teaching or suggestion of all the claim limitations, no reasonable expectation of success with respect to the instant claimed invention, nor any motivation to arrive at the instant claimed invention, a method for assessing cardiac or skeletal muscle damage. Accordingly, the cited combination of references by Solaro et al., Lin et al. and Han et al. cannot render *prima facie* obvious the instant claims drawn to methods for assessing cardiac or skeletal muscle damage.

Further, the secondary references of Wicks et al. and Wicks et al. further in view of Jideama et al., cited in the rejection of dependent claims 2-7, 28, 34-35, 38 and 40-41 and dependent claims 37 and 39, respectively, fail to remedy the deficiencies in the combined teachings of Solaro et al., Lin et al. and Han et al.

With respect to the rejection of claims 2-7, 28, 34-35, 38 and 40-41, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the

invention was made "to measure two different myofilament product degradation products (troponin I and troponin C) in muscle damage as taught by Wicks et al. in the method of Solaro et al. in view of Lin et al. and further in view of Han et al. because Wicks et al. taught that troponin I is one of three subunits of the troponin complex." However, the claims are not drawn to assessing cardiac and skeletal muscle damage via detecting the presence of troponin I and troponin C, but rather to assessing cardiac and skeletal muscle damage via detecting the presence of a **post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins selected from the group consisting of troponin I, troponin T, troponin C, α-actinin and myosin light chain 1.** Thus, the cited combination of references of Solaro et al., Lin et al. and Han et al. (none of which relate to assessing muscle damage), in further view of Wicks et al., which is unrelated to detecting the presence of any of the myofilament protein modification products claimed, clearly fails to provide the requisite reasonable expectation of success with respect to the instant claimed method for

assessing cardiac or skeletal muscle damage based upon detecting the presence of these myofilament protein modification products and the requisite teaching or suggestion of all the claim limitations. Accordingly, the cited combination of references by Solaro et al., Lin et al. and Han et al. and further in view of Wicks et al. cannot render *prima facie* obvious the instant claims drawn to methods for assessing cardiac or skeletal muscle damage via detecting the presence of a post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins selected from the group consisting of troponin I, troponin T, troponin C, α-actinin and myosin light chain 1.

With respect to the rejection of claims 37 and 39, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to measure myofilament protein degradation products involving phosphorylation states as taught by Jideama et al. in the method of Solaro et al. in view of Lin et al. and further in view of Han et al. and Wicks et al. because Jideama et al. taught that the phosphorylation state and

properties of myofilament proteins were time dependent relating to phosphorylation extent, substrate affinity and inhibitions.

However, like Solaro et al., Lin et al. and Han et al., Jideama et al. are silent with respect to any teaching whatsoever concerning assessing cardiac or skeletal muscle damage. Thus, the cited combination of Solaro et al., Lin et al. and further in view of Han et al. and Wicks et al. and further in view of Jideama et al. still fails to provide the requisite reasonable expectation of success with respect to the instant claimed method for assessing cardiac or skeletal muscle damage based upon detecting the presence of a post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins selected from the group consisting of troponin I, troponin T, troponin C, α-actinin and myosin light chain 1 as well as the requisite teaching or suggestion of all the limitations of the instant claims. Accordingly, the cited combination of Solaro et al., Lin et al. and further in view of Han et al. and Wicks et al. and further in view of Jideama et al. also fails to establish a prima facie case of

obviousness with respect to the instant claimed method for assessing cardiac and skeletal muscle damage.

Withdrawal of these rejections under 35 U.S.C. 103(a) is therefore respectfully requested.

II. Provisional Obviousness-type Double Patenting Rejection

Claims 1-7, 16-18, 20-28, 31, 34-35 and 37-41 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 80-98 of copending U.S. Application No. 09/115,589.

Claims 37 and 39 have also been rejected under the judicially created doctrine of obviousness-type double patenting over claims 80-98 of copending U.S. Application No. 09/115,589 in view Jideama et al. (Journal of Biological Chemistry, Vol. 271, No. 38, 9/20/96, 23277-23283).

Applicants respectfully traverse these rejections.

In accordance with MPEP 804, the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection. Thus, to render claims 1-7, 16-18, 20-28, 31, 34-35 and 37-41 obvious, claims 80-98 of copending U.S. Application No. 09/115,589 alone or in combination with Jideama et al. must provide some suggestion or motivation to modify and/or

combine their teachings, a reasonable expectation of success, and a teaching or suggestion of all the claim limitations.

Claims 80-98 of copending U.S. Application No. 09/115,589 are drawn to a method for assessing skeletal muscle damage in a subject via detection of a **peptide fragment** of a myofilament protein or a covalent or non-covalent complex of at least a **peptide fragment of a myofilament protein and an intact myofilament protein** or **two peptide fragments** of myofilament proteins wherein the myofilament protein is skeletal troponin I peptide fragments, or skeletal troponin T peptide fragments.

In contrast, claims of the instant application are drawn to a method for assessing cardiac and skeletal muscle damage in a subject via detection of a **chemical adduct** of a myofilament protein, which is stated in the claims to be a **post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins** and said myofilament protein is selected from the group consisting of troponin I, troponin T, troponin C, α-actinin and myosin light chain 1.

Claims of copending U.S. Application No. 09/115,589 relating to detection of a **peptide fragment** of a myofilament protein or a covalent or non-covalent complex of at least a **peptide fragment** of a myofilament protein and an intact myofilament protein or two **peptide fragments** of myofilament proteins in assessing skeletal muscle damage are no way suggestive or predictive of **chemical adducts** of a myofilament protein, and in particular post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins being indicative of cardiac and skeletal muscle damage.

Thus, the claims of copending U.S. Application No. 09/115,589 clearly fail to provide the requisite motivation, reasonable expectation of success with respect to the instant claimed invention, and suggestion of all claim limitations to render the instant invention obvious.

Teachings of the secondary reference by Jideama et al. fail to remedy deficiencies in the primary reference as Jideama et al. is silent with respect to post-translationally modified proteins being indicative of cardiac and skeletal muscle damage.

Withdrawal of these rejections under the judicially created doctrine of obviousness-type double patenting is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

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Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053
(856) 810-1515